

US006506559B1

(12) United States Patent

Fire et al.

(10) Patent No.:

US 6,506,559 B1

(45) Date of Patent:

*Jan. 14, 2003

(54) GENETIC INHIBITION BY DOUBLE-STRANDED RNA

(75) Inventors: Andrew Fire, Baltimore, MD (US);
Stephen Kostas, Chicago, IL (US);
Mary Montgomery, St. Paul, MN
(US); Lisa Timmons, Lawrence, KS
(US); SiQun Xu, Ballwin, MO (US);
Hiroaki Tabara, Shizuoka (JP);
Samuel E. Driver, Providence, RI
(US); Craig C. Mello, Shrewsbury, MA
(US)

(73) Assignce: Carnegie Institute of Washington, Washington, DC (US)

(*) Notice: This patent issued on a continued prosecution application filed under 37 CFR 1.53(d), and is subject to the twenty year patent term provisions of 35 U.S.C. 154(a)(2).

Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: 09/215,257

(22) Filed: Dec. 18, 1998

Related U.S. Application Data

(60) Provisional application No. 60/068,562, filed on Dec. 23, 1997.

(56) References Cited

U.S. PATENT DOCUMENTS

4,469,863 A	9/1984	Ts'o et al.
4,511,713 A	4/1985	Miller et al.
5 034 323 A	7/1991	Jorgensen et al

5,107,065	Α	4/1992	Shewmaker
5,190,931	Α	3/1993	Inouye
5,208,149	Α	5/1993	Inouye
5,258,369	Α	11/1993	Carter
5,272,065	Α	12/1993	Inouye
5,365,015	Α	11/1994	Grierson et al.
5,453,566	Α	9/1995	Shewmaker
5,738,985	Α	4/1998	Miles
5,795,715	Α	8/1998	Livache
5,874,555	Α	2/1999	Dervan
5,972,704	Α	* 10/1999	Draper et al.
6,010,908	Α	1/2000	Gruenert et al.
6,136,601	Α	10/2000	Meyer, Jr. et al.

FOREIGN PATENT DOCUMENTS

WO	94/01550	* 1/1994
wo	WO 99/32619	7/1999
wo	WO 99/53050	10/1999
wo	WO 99/61631	12/1999
wo	WO 00/01846	1/2000
WO	WO 00/63364	10/2000

OTHER PUBLICATIONS

Sharp, 1999. Genes and Development, 13:139-141.* Clemens. et al., May 23, 2000. Proc Natl Acad Sci, early edition, http://www.pnas.org/cgi/doi/10.1073/ pnas.110149597.*

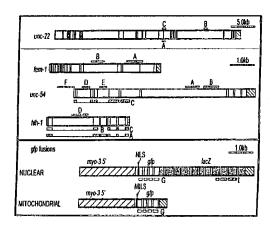
(List continued on next page.)

Primary Examiner—Andrew Wang
Assistant Examiner—Karen A Lacourciere
(74) Attorney, Agent, or Firm—Morgan, Lewis & Bockius
LLP

(57) ABSTRACT

A process is provided of introducing an RNA into a living cell to inhibit gene expression of a target gene in that cell. The process may be practiced ex vivo or in vivo. The RNA has a region with double-stranded structure. Inhibition is sequence-specific in that the nucleotide sequences of the duplex region of the RNA and of a portion of the target gene are identical. The present invention is distinguished from prior art interference in gene expression by antisense or triple-strand methods.

22 Claims, 5 Drawing Sheets



435/91.1, 325

